pointing to the probability that there are certain nerve fibres which do not depend on the ganglion for their trophic supply, but derive the same from elsewhere, either the spinal cord at another level, or the periphery.

In conclusion, the author calls special attention to the value of the method of excluding one or more nerve roots during an epileptic spasm, as affording a means of confirming the facts that have been previously observed from stimulation of the nerve roots, and also of ascertaining new facts with regard to them and the plexuses which they form. He further goes on to point out that it supplies a valuable means of studying the manner in which conduction of impulses from the cortex through the nerve roots and plexuses to the muscles takes place; and that it is capable of still wider extension, as if, instead of producing general epilepsy, less powerful stimuli be applied to the centres for different movements, as represented in the motor cortex, it will afford a means of connecting such centres, or parts of these, with the nerve roots to which fibres proceed from these cortical motor centres.

III. "The Influence of the Kidney on Metabolism." By J. Rose Bradford, M.D., D.Sc., Fellow of University College, London, Assistant Professor of Clinical Medicine at University College, Grocer Research Scholar. Communicated by Professor Schäfer, F.R.S. Received February 18, 1892.

(From the Physiological Laboratory of University College, London.)

The results described in this preliminary communication were obtained in a series of experiments commenced in June, 1889, and at present still in progress, with the object of elucidating the functions of the kidneys, and to gain an insight into the disturbance produced in the economy by disease of these organs.

Method.—All the experiments were made on dogs, and a complete experiment involves the following stages:—

Firstly.—The animal, after being weighed, is placed in a suitable chamber, and fed on a weighed diet containing a known quantity of nitrogen; the water drunk is also measured. The amount of urine passed is measured, and the quantity of urea and total nitrogen in it determined. Finally, the weight of the fæces and the amount of nitrogen in them are also determined. All the nitrogen determinations were made by means of Kjeldahl's method; the urea was estimated by the hypobromite method. A daily determination of the above factors was made for a period of a week, and a daily average

thus obtained. In the earlier experiments only the quantities of urine and urea passed were determined. On removal from the chamber, the animal is again weighed.

Secondly.—The operation described below is performed on one kidney. After recovery from this, the dog is again placed in the collecting chamber, and the above data again obtained for a week or more.

Thirdly.—The second kidney is removed, and the animal again placed in the collecting chamber, the food and excreta being again determined for a period of a week or more.

Fourthly.—At a variable time after the second operation the animal is killed by bleeding, and the amount of nitrogenous extractives present in the tissues determined.

As regards the operative procedures, there is nothing to remark about the second operation—the kidney is removed in the usual manner by lumbar incision; a few words are necessary in order to describe the first operation. After anæsthetising the animal with chloroform and morphia, the kidney is exposed by a lumbar incision and freed from its connexions. The vessels in the hilus are then compressed with the fingers, the kidney transfixed from before back, and a large wedge of kidney substance, with the apex of the wedge at the pelvis of the kidney, removed from the middle of the organ. The piece removed weighed from 5 to 15 grams in different cases. The very free hæmorrhage is arrested by ligature of the large vessels divided, and by pressure on the cut surface. When all bleeding had been arrested (the vessels in the hilus being of course no longer compressed) the cut surfaces of the kidney were brought together by two or three silk sutures passed in deeply, and by numerous superficial fine horsehair sutures involving only the cortex and capsule of the organ. The abdominal wound was closed and dressed in the usual manner.

Full antiseptic precautions were always used, and morphia was given hypodermically to prolong the narcosis.

Summary of Experiments.—Twenty-three animals survived the first operation: fifteen animals survived both operations.

Thus, eight animals died after the first operation and before the second. The causes of death in these eight were as follows:—

In four cases the animals were accidentally killed with chloroform administered to perform the second operation. In two cases the wound became septic and the animals were killed. In one case death resulted from hæmorrhage on the seventh day, and one dog, to which further reference will be made below, died of asthenia thirty-six days after the first operation.

This communication deals with the results obtained in the fifteen complete experiments. In one, the first, no observations were made on the urine, and in three dogs the observations were incomplete, so

that there remain eleven cases in which observations were made on the urine before and after the operations.

Effects of the First Operation (*i.e.*, the removal of a wedge of the kidney substance).—The shock of the operation passes off in about twenty-four hours, but for two or three days there is some hæmaturia, and the appetite is poor. The temperature of the body remains at its normal height, or there may be slight pyrexia. The dog, however, soon regains its former health, and no permanent ill effects result from the operation in the great majority of cases. In one case (one of the eight incomplete experiments) the animal died thirty-six days after the operation, with considerable wasting and loss of appetite, and nothing was found *post mortem* except extreme atrophy of the kidney operated on. The opposite kidney was healthy and of normal size. The atrophy was very marked, as the following numbers show:—7·6 grams of the left kidney were removed, *post mortem* the remaining fragment of the left kidney weighed only 3·5 grams, and the opposite kidney 18 grams. In this case, the only one where death resulted from the effects of the first operation, although the atrophy was very marked, there was microscopically no evidence of cirrhosis, and no lesions of the renal vessels were discovered. The cause of death is obscure, as the second kidney was not removed.

With this one exception, the first operation failed to produce any serious or permanent ill effects, and the only result noticed was slight emaciation, but this was generally recovered from in a week or two.

A period of from one to six weeks was allowed to elapse between the first and second operations, and during this time the animal was placed in the chamber, and the ingesta and excreta determined. The following table gives the results observed in five cases:—

Table I.

Weight of dog.	Daily quantity of urine.		Daily quantity of urea.		Weight of kidney removed.	Interval between operation and observation.	Loss in weight of dog.
	Before operation.	After operation.	Before operation.	After operation.			
No. 16, 16 lbs.	166 c.c.	200 c.c.	7 grams	10 grams	6 grams	16 days	1·5 lbs. in 36 days
No. 21, 13 lbs.	113 c.c.	98 c.c.	9 grams	8 grams	7 grams	15 days	1 lb. in 28 days
No. 22, 14 lbs.	86 c.c.	156 c.c.	5 grams	7 grams	5 grams	35 days	2 lbs. in 39 days
No. 23, 11 lbs.	115 c.c.	140 c.c.	16 grams	15 grams	6·5 grams	14 days	1 lb. in 34 days
No. 24, 15 lbs.	130 c.c.	128 c.c.	16 grams	14 grams	10 grams	16 days	1 lb. in 21 days

From this tabular statement of the results in five cases it will be seen that, as stated above, the results of the operation are trifling when we consider its severity. In one case, No. 16, the output of urea was increased from 7 to 10 grams per diem. In this case the ingesta were not determined, and the apparent increase may have been due to an increased diet. In No. 22 the diet was the same before and after the operation, but there is an increase in the urine and urea after the operation. This case is quoted because it illustrates the maximum effect produced; in no other case was so great an effect observed. In the other cases the effects on the urine, &c., are so slight as to be well within the limits of experimental errors. The loss in body weight is trifling when compared with that described below as resulting from the second operation. The greatest loss observed was in Dog 22, where the body weight fell from 14 lbs. to 12 lbs. The specific gravity of the urine is not permanently affected by the operation. In the first few days after the operation, whilst there is hæmaturia, the urine is frequently more abundant in quantity and the specific gravity then is temporarily lowered, but this soon passes off, and the urine returns to its normal quantity and density.

The Results following the Second Operation.

The results following the removal of the second kidney differ widely from those described above as following the first operation, in that there are frequently no immediate ill effects, the animal running about, &c., within a few hours of the nephrectomy, and there is but little shock, hæmorrhage, &c., when compared with the first operation. The remote effects, however, are very marked: a widespread disturbance of nutrition ensues, accompanied by extreme wasting, hydruria, and polyuria, and with these a fall in the body temperature and a great increase in the nitrogenous extractions of the tissues, provided a sufficiently large amount of kidney has been removed at the first operation.

In all cases the wound has healed up rapidly and soundly, and in no case has death resulted directly from the operation. Out of the fifteen experiments, the first was killed five days after the second operation, and at that time the animal was in sound health. In four cases, No. 2, No. 11, No. 19, and No. 21, the animals were killed 47 days, 60 days, 14 days, and 30 days respectively after the second operation, and the results observed in them will be described below (*vide* Table IV). In the remaining ten cases the dogs either died of a rapidly progressive asthenia, or else they were killed at a time when they were practically moribund.

The results in four cases out of the ten are given in the following table:—

Table II.

Weight of dog.	Daily quantity of urine.		Daily quantity of urea.		Weight of kidney removed at 1st operation.	Weight of 2nd kidney also removed.	Weight of kidney found *post mortem*.	Amount of kidney removed expressed as a fraction of total kidney weight.
	Before 2nd operation.	After 2nd operation.	Before 2nd operation.	After 2nd operation.				
No. 6, 11 lbs.	127 c.c.	270 c.c.	4·5 grams	10·2 grams	7·4 grams	24·4 grams	10·5 grams	$\frac{3}{4}$
No. 9, 15 lbs.	260 c.c.	450 c.c.	9 grams	16·8 grams	6·7 grams	27 grams	12 grams	$\frac{3}{4}$
No. 12, 19 lbs.	157 c.c.	458 c.c.	8·6 grams	13·6 grams	8 grams	30 grams	12 grams	$\frac{3}{4}$
No. 23, 11 lbs.	115 c.c.	550 c.c.	16 grams	21 grams	6·5 grams	22 grams	10 grams	$\frac{3}{4}$

From this table it will be seen that the second operation is followed by a great increase in the amount of urine excreted, and also by a large increase in the output of urea. The increase in the urinary water, however, is greater than the increase in the urea, although the latter, as seen above, is greatly augmented.

This condition of polyuria is accompanied by great wasting.

Thus the weight of	Dog	No.	6	fell from	11	lbs. to	8	lbs. in	50 days.
,,	,,	No.	9	,,	15	,,	10	,,	18 ,,
,,	,,	No.	12	,,	19	,,	12	,,	15 ,,
,,	,,	No.	23	,,	11	,,	7	,,	25 ,,

This wasting is rapid in its course, and is not materially checked by a liberal diet, when the animal's appetite will admit of it. The appetite frequently fails somewhat, but the animals will eat meat in large quantities to within a short time of their death, although they refuse dog biscuit. There is also great thirst, and this, no doubt, is in close relation with the hydruria. When the polyuria is fully established, the rectal temperature falls, so that ultimately it may be as low as 97° F., or even 95° F., the normal temperature varying between 101° F. and 102° F. This condition of polyuria leads to a more or less rapid death; all the animals in Table II either died, or were killed because moribund, in from two to six weeks after the second operation.

The following table gives the results in the remaining six cases out of the ten rapidly fatal cases: —

Table III.

Weight of dog.	Daily quantity of urine.		Daily quantity of urea.		Weight of kidney removed at 1st operation.	Weight of 2nd kidney also removed.	Weight of kidney found *post mortem*.	Amount of kidney removed expressed as a fraction of total kidney weight.
	Before 2nd operation.	After 2nd operation.	Before 2nd operation.	After 2nd operation.				
No. 3, not observed	not observed	381 c.c.	not observed	11 grams	15 grams	28·4 grams	15 grams	$\frac{3}{4}$
No. 4, 16 lbs.	not observed	230 c.c.	not observed	not observed	10·4 grams	25·5 grams	13·6 grams	$\frac{3}{4}$
No. 5, not observed	225 c.c.	330 c.c.	9 grams	more than 8 grams	6·4 grams	19 grams	5·5 grams	$\frac{5}{6}$
No. 14, 14 lbs.	187 c.c.	393 c.c.	11·6 grams	11·4 grams	8 grams	19·5 grams	8·2 grams	$\frac{3}{4}$
No. 22, 14 lbs.	86 c.c.	150 c.c.	5 grams	5·5 grams	5 grams	18·5 grams	10 grams	$\frac{2}{3}$
No. 28, 13 lbs.	92 c.c.	311 c.c.	9 grams	8 grams	10 grams (about)	23 grams	7·8 grams	$\frac{4}{5}$

In *all* these cases it is seen that the amount of urine excreted after the second operation is very large, and in all the cases where the amount of urine was also determined before the operation it is found that the latter daily quantity is far less. In only four out of the six cases was the daily output of urea investigated both before and after the operation. In Dog No. 5 the urea was apparently decreased in amount, but in reality it must have been greatly increased, as, owing to a mistake and absence from the laboratory, the urines, after the operation, were put aside for several days, and only tested when putrefaction had taken place; hence the real amount was probably far greater than 8 grams. In the other three cases, the output of urea was either slightly diminished or slightly increased; this result is of considerable interest from the fact that these dogs ate little or nothing after the operation. Thus, No. 22 passed 5 grams of urea daily with a diet of 230 grams of dog biscuit; after the operation 5·5 grams of urea were excreted, but no food was taken, the animal refusing to eat the biscuit.

In No. 28, 9 grams of urea were excreted per diem with 100 grams of meat and 100 grams of biscuit daily; after the operation 8 grams of urea, with the ingesta diminished to 40 grams of meat and 20 grams of biscuit daily. Similarly, in No. 14, a liberal allowance of meat and biscuit were given and eaten before the operation, but after only small quantities of meat were eaten, and often none at all. The comparatively small quantity of urea excreted in these cases, when compared to the instances given in Table II, is not dependent upon any inability on the part of the fragment of kidney left to excrete urea. This is well shown by the following observation on No. 22. This dog, as just mentioned, excreted only 5·5 grams of urea per diem with no ingesta; but, on a diet of 200 grams of meat, the daily output of urea rose immediately to an average of 15 grams, and on some days as much as 19 grams were excreted by a fragment of kidney found on post-mortem examination to weigh only 10 grams. Hence, even in the cases where the urea is not absolutely largely increased, it is really increased when we remember that the ingesta are greatly diminished, and that the dog may pass as much, or even more, urea during a whole week with no food as the animal previously passed on a full diet, *e.g.*, No. 22. In all six cases described in Table II the operation was followed by death in from one to four weeks.

It is to be noted that in all the ten cases summarised in Tables II and III, the total amount of kidney substance removed amounted to some three-fourths or more of the total kidney weight, with one exception, where only two-thirds was removed. In all these ten cases there were emaciation, hydruria, and polyuria, absolute or relative.

Table IV.

Weight of dog.	Daily quantity of urine.		Daily quantity of urea.		Weight of kidney removed at 1st operation.	Weight of second kidney, also removed.	Weight of kidney found *post mortem*.	Amount of kidney removed expressed as a fraction of total kidney weight.
	Before 2nd operation.	After 2nd operation.	Before 2nd operation.	After 2nd operation.				
No. 2, 21 lbs.	Not observed	342 c.c.	Not observed	15 grams	10 grams	42 grams	28·5 grams	$\frac{2}{3}$
No. 11, 14 lbs.	132 c.c.	313 c.c.	10 grams	12·5 grams	8 grams	25·4 grams	18 grams	$\frac{2}{3}$
No. 19, 13·5 lbs.	140 c.c.	286 c.c.	9 grams	10 grams	5·7 grams	26·2 grams	14 grams	$\frac{2}{3}$
No. 21, 12 lbs.	113 c.c.	200 c.c.	9 grams	7·5 grams	7 grams	22 grams	16 grams	$\frac{2}{3}$

In the remaining four dogs described in Table IV the amount of kidney removed was slightly less, and, as the table shows, the results are different to those described in the ten rapidly fatal cases.

In none of these cases was the operation fatal, and, as previously mentioned, the animals were killed 47 days, 60 days, 14 days, and 30 days respectively after the second operation. In no case was there any great emaciation, the greatest loss of weight being in No. 11, where the body weight fell from 14 lbs. to 12 lbs. In all cases there was marked hydruria, but the polyuria was slight or absent, notwithstanding the fact that there was no failure of appetite. Thus these four experiments are in great contrast to the other ten, where a larger amount of kidney was removed with a uniformly fatal result. It is clear from these results that the increased flow of urine is not dependent simply upon any increased excretion of urea, since the former may exist without the latter. In no case, however, has an increased excretion of urea been obtained without an increase in the quantity of urine.

In no case amongst the ten fatal ones (where three-fourths of the total kidney weight was removed) has the operation been followed by a diminution in the output of urea, provided the ingesta were not diminished.

We may then form the following conclusion, that when a dog is left with only one-fourth of its total kidney weight, a condition of extreme hydruria invariably results. This hydruria is accompanied, provided the appetite does not fail, by a large increase in the output of urea. Further, that if the ingesta are diminished even to zero, the output of urea remains at the height it reached with a diet sufficient to maintain the weight of the animal when in a normal condition.

That the hydruria, although associated with an increased excretion of urea, is not dependent upon it, is shown not only by the fact mentioned above, that by removal of a smaller amount of kidney hydruria pure and simple is produced, but also by the fact that when both hydruria and polyuria are produced they do not begin simultaneously. In other words, when hydruria and polyuria are both ultimately produced by removal of three-fourths of the total kidney weight, the hydruria *precedes* the polyuria. To illustrate this, it will be sufficient to quote one experiment, *i.e.*, No. 23. After the first operation, when 6·5 grams of the left kidney were removed, the dog passed 140 c.c. of urine containing 15 grams of urea per diem, with a diet of 150 grams of meat. On increasing the food to 200 grams of meat per diem, the urine rose to 212 c.c., containing 17 grams of urea. The second kidney, weighing 22 grams, was then removed. In the week following the operation the ingesta fell to 120 grams, and the urea to 13 grams per diem, the urine rising to 380 c.c. In the second week

the appetite was regained, the ingesta returned to 200 grams, the urea rose to 16 grams, and the urine to 480 c.c. In the third week the ingesta were 140 grams, the urea rose to 21 grams per diem, and the urine to 550 c.c.; the animal was then killed, being weak, the body weight having fallen from 11 lbs. to 7 lbs. This experiment illustrates the two stages the animals pass through, the first one where the normal output of urea is maintained, but the method of its excretion is altered, so that the quantity of urinary water is greatly increased. The second stage is one where the quantity of urine is still further increased, with a more or less sudden increase in the urea, accompanied by emaciation, &c. By the removal of very large quantities of kidney substance these two results are obtained almost together, but even then, for a day or two after the second operation, hydruria only is present. When, however, a smaller quantity of kidney is removed the condition called here the first stage is the only one produced, and this condition of simple hydruria is very permanent, as the experiments quoted in Table IV demonstrate. My observations do not show whether this stage of hydruria can be prolonged indefinitely, but they show that the second stage, polyuria, emaciation, is comparatively sudden in its onset, and rapid in its course.

Character of the Urine.—The urine passed after the second operation contrasts greatly with the normal urine of the dog, inasmuch as it is very pale, abundant, and of low specific gravity, *i.e.*, from 1007 to 1020; whereas the normal urine is dark in colour, and its specific gravity is often as high as 1050 or even 1060, and it is scanty in amount. The urine after the second operation contains neither albumen nor sugar. The percentage of solid matter is of course less than normal, but the total solids are not diminished in amount. The ash also is not diminished; but more detailed observations on these points are at present in progress.

With regard to other symptoms of the disorder produced by the operation, it is to be noted that convulsions are absent. Vomiting is rare; it has only been observed once or twice. Diarrhœa is frequently present towards the end, and small ulcers and sores occur about the lips and feet, possibly of traumatic origin. During the last twenty-four or forty-eight hours of life the flow of urine diminishes greatly, so that usually the animals have been killed whilst the polyuria, &c., was at its height, so as not to vitiate the analysis of the tissues. Thus the final symptoms are great prostration of strength and some drowsiness, together with the great fall in the temperature; the last, however, begins as soon as the polyuria is marked, and hence is present for many days before death.

The aortic blood pressure, measured by connecting the carotid artery to a mercurial manometer, is very high when the marasmic condition of the animal is considered. In three cases observed it

has varied between 95 and 100 mm. Hg, the animal being under the influence of chloroform, that is to say, the blood pressure was as high as it frequently is in normal and healthy chloroformed dogs. This height of the blood pressure is in great contrast to the blood pressure in dogs after double nephrectomy, where even on the third day the blood pressure has sunk to a few millimetres of mercury.

Hence the arterial tension is raised when the animal has but $\frac{1}{3}$rd to $\frac{1}{4}$th of its total kidney weight.

Post-mortem Examination.—The animals are greatly emaciated, but usually some fat remains, especially the omental fat. No marked naked-eye changes have been detected, except a marked excess of cerebro-spinal fluid in the cranial cavity. No obvious change was found in the heart or vessels. The abdominal viscera have been found rather soft and sticky, but no other evidence of septic poisoning or of auto-infection has been found.

The kidney fragment has never been found hypertrophied; more frequently distinctly atrophied, the weight of the fragment found *post mortem plus* the weight of the piece removed being generally less than the weight of the opposite kidney. This is in opposition to the results of a French observer.* He, however, removed at the first operation the entire kidney, and then subsequently removed pieces of the second kidney, which had, as is well known, undergone a so-called compensatory hypertrophy. Under these circumstances Tuffier states that the fragment hypertrophies considerably.

Whether the atrophy observed by me is dependent upon the part of the kidney removed, I trust to elucidate by further observations now in progress.

Nitrogenous Extractives of the Blood and Tissues.—The animals, after being anæsthetised with chloroform, were bled to death. 50 c.c. of blood were placed in an excess of rectified alcohol and 50 grams of muscle, liver, brain were similarly treated after being finely divided. After prolonged extraction, the filtrate is then evaporated to dryness over a water-bath, and the dry residue repeatedly extracted with cold absolute alcohol, usually for some hours. The absolute extract is evaporated to dryness on the water-bath and the residue dissolved in water. The material insoluble in absolute is also dissolved in water, and thus two watery extracts are obtained which may, for simplicity, be called the absolute and rectified extract; these are treated as follows:—half of each is introduced separately into a Dupré urea apparatus, and the amount of nitrogen evolved by decomposition with sodium hypobromite determined. In the remaining half of each extract the total nitrogen present was determined by Kjeldahl's method. In this manner a control is kept on the hypobromite method, since, if such a body as urea is present, the Dupré and

* Tuffier, 'Études expérimentales sur la Chirurgie du Rein,' Paris, 1889.

Kjeldahl determinations should nearly coincide, whereas, if such a body as creatin, &c., is present, the one method would yield twice as much nitrogen as the other. In the present communication only the extractives present in what has been called above the "absolute extract" will be considered, and the results obtained in four experiments are given below. In two cases, No. 19 and No. 21, the removal of two-thirds of the kidney weight had produced simple hydruria, and in the other two cases, No. 23 and No. 28, a more extensive operation had produced polyuria as well. In 23, the polyuria was absolute, in 28 relative, the ingesta being diminished in the latter but not in the former.

It is to be distinctly understood that in the following results the extractive is reckoned on urea, because of its solubility in cold alsolute alcohol, and because the amount of nitrogen obtained by the Dupré and Kjeldahl methods respectively practically coincided.

	Blood.	Muscle.	Liver.	Brain.
No. 19.....	0·065 p.c.	0·030 p.c.	nil	0·04 p.c.
No. 21.....	0·045 „	0·035 „	0·024 p.c.	0·03 „
No. 23.....	0·410 „	0·430 „	0·200 „	0·24 „
No. 28.....	0·360 „	0·300 „	0·200 „	0·22 „

No. 23 was passing an average of 21 grams of urea per diem at the time of death, and No. 28 an average of 8 grams, although in the latter case 10·6 grams of urea were excreted in the last twenty-four hours of life. From these results we see that in the case of dogs suffering from the simple hydruria, the amount of "urea" in the blood and tissues is only slightly above the normal. In the case of the dogs in the second stage, suffering from polyuria, &c., the amount of "urea" in the blood and tissues is enormously increased. Thus, in No. 23 at least twenty times the normal quantity of "urea" was present in the blood, at a time when the animal was still excreting an amount greatly exceeding the normal (*vide* Table II). Hence the excess of extractive matter present in the tissues is not dependent on simple retention, but on increased production.

I trust to consider the extractives soluble in rectified alcohol in a future communication, but they also are largely increased in the tissues, but not in the blood.

The specific gravity of the blood serum is lower than normal, sinking frequently to 1025. The total solids, the proteids, and the ash of the serum are all diminished in amount, the last falling to 0·5 per cent. in many cases.

The disturbance of nutrition with increased production of urea

described above does not follow destruction of the renal plexus, nor does it follow free incision of the kidney with subsequent suturing of the damaged organ. It is a phenomenon closely connected with the removal of *large* quantities of kidney, *i.e.*, half of one kidney and the whole of the second. Inasmuch as the phenomena do not ensue after the first and more severe operation, but only after the second and comparatively trivial operation, it must be concluded that they are more related to the *quantity* of kidney removed than to the shock of the operation, or to any reflex disturbance produced by the operation.

The excess of urea in the muscle over that in the liver and brain might be considered as evidence of its production in the muscles. That this is not necessarily the case is shown by the results of the injection of large quantities of urea into the circulation of normal dogs. The dogs were anæsthetised with chloroform, the ureters ligatured, and the urea then injected into the external jugular. After from one to three hours the animals were killed by bleeding, and the tissues examined, as described above.

Dog's weight.	Amount of urea injected.	Time.	Amount of urea in			
			Blood.	Muscle.	Liver.	Brain.
20 lbs.	10 grams.	2¾ hours.	0·11 p.c.	0·08 p.c.	0·04 p.c.	?
13·5 lbs.	20 grams.	1½ hours.	0·25 p.c.	0·35 p.c.	0·22 p.c.	0·2 p.c.

From these and other observations, we see that the percentage of urea in the muscles is greater than in the case of the liver and brain after intravenous injection, and that it may exceed that of the blood. The smaller percentage in the liver is not dependent upon the excretion of urea through the bile duct, because after ligature of the bile duct the percentage in the liver is still lower than that of the muscles after the intravenous injection of urea. After ligature of both ureters, and after double nephrectomy, the same distribution of urea is found in the tissues.

In all the following cases the animals were killed three days after the operation.

The large quantity of urea present in the muscles under all these different circumstances cannot as yet be regarded as evidence of its direct production in the muscles.

Dog's weight.	Operation.	Blood.	Muscle.	Liver.	Brain.
13 lbs.	Ligature of ureters	0·3 p.c.	0·22 p.c.	0·18 p.c.	?
20 lbs.	Ligature of ureters	0·37 p.c.	0·42 p.c.	0·38 p.c.	0·23 p.c.
12 lbs.	Double nephrectomy	0·34 p.c.	0·32 p.c.	0·18 p.c.	0·17 p.c.

Finally, in the tissues of patients dying from uræmia consequent on cirrhosis of the kidney, very large quantities of urea have been found by me, and here also the percentage in the muscles has been much higher than in the liver. This conclusion is based on the examination of the tissues in fourteen cases.

Presents, March 3, 1892.

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